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N-CYCLOAMINO-SUBSTITUTED POLYFLUORINATED SALICYLIC ACIDS AND THEIR BIOLOGICAL ACTIVITY

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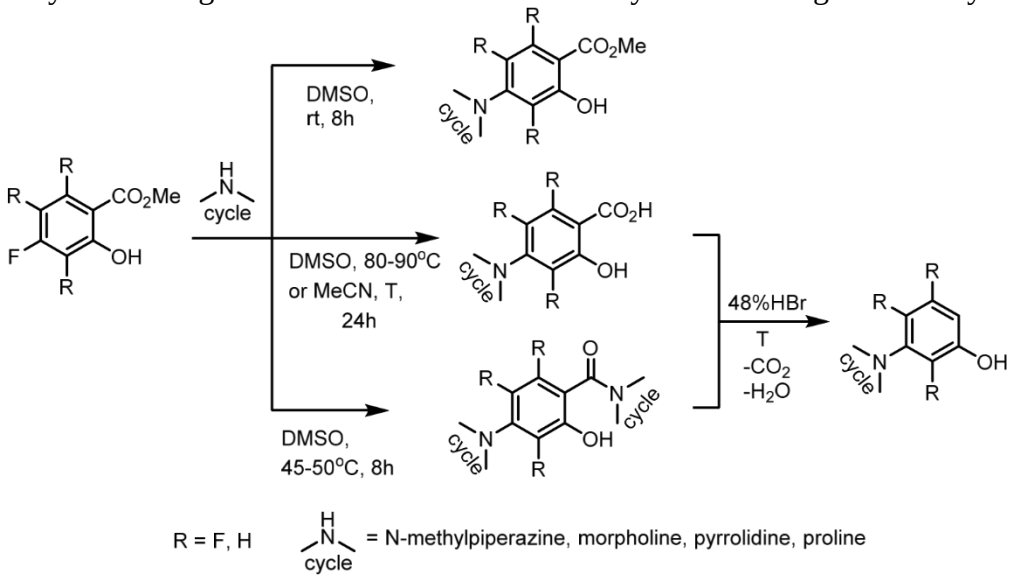
Abstract. Earlier, we have developed a convenient method for polyfluorosalicylic acids synthesis *via* hydrolysis of *ortho*-methoxypolyfluorobenzoic acids which were obtained by the effective protocol of selective *orthomono*-methoxylation of commercially available polyfluorobenzoic acids.[1] It was synthesized fluorinated analogues of the known drugs of salicylic group based on polyfluorosalicylic acids.[2] Fluorosalicylates were evaluated *in vivo* tests on anti-inflammatory and analgesic actions. It was revealed the high activity of tri- and tetrafluorosalicylic acids but in combination with an acute toxicity. We proposed to solve the problem of high toxicity of polyfluorosalicylates due to nucleophilic aromatic *ipso*-substitution of fluorine for pharmacophore nitrogen-containing moiety. We used the following amines:
N-methylpiperazine, morpholine, pyrrolidine and proline.[3] The attempts to carry out the nucleophilic substitution of polyfluorosalicylic acids with the secondary amines unsuccessful because the salt formation seemed to occur. Their esters were readily undergone the substitution at fluorine in the position 4 on amine fragment. It was realized amidation, hydrolysis and decarboxylation of esters depending on the conditions. The introduction of cycloamine moiety into polyfluorosalicylic acids was found to lead to reduce of toxicity without significant loss of anti-inflammatory and / or analgesic activity.



References

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